

Application No.: 10/622,320
Response dated March 6, 2006
Reply to Office Action of September 6, 2005

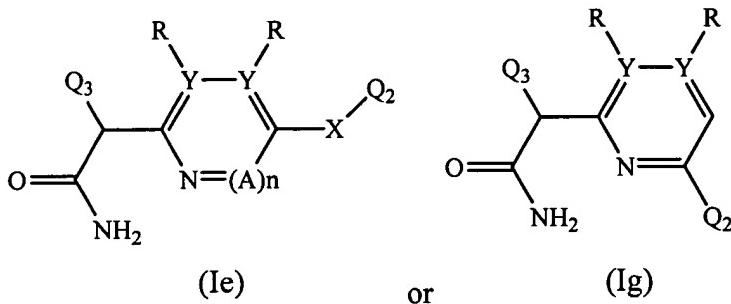
AMENDMENTS TO THE CLAIMS

Claims 3, 8-15, 18-23, and 25-37 are currently pending. Please cancel claims 13-14, 30-33, and 35-37. Please amend claims 3, 10, 11, 26-29, and 34, as indicated below. This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing Of Claims

1-2. (Canceled)

3. (Currently Amended) A compound of the formula:



wherein:

Q_3 is a 5-6 membered aromatic carbocyclic or heterocyclic ring system; or an 8-10 membered bicyclic ring system comprising aromatic carbocyclic rings, aromatic heterocyclic rings or a combination of an aromatic carbocyclic ring and an aromatic heterocyclic ring; wherein Q_3 is substituted with 1 to 4 substituents, each of which is independently selected from halo; C_1 - C_3 alkyl optionally substituted with NR'_2 , OR' , CO_2R' or $CONR'_2$; $O-(C_1-C_3)$ -alkyl optionally substituted with NR'_2 , OR' , CO_2R' or $CONR'_2$; NR'_2 ; OCF_3 ; CF_3 ; NO_2 ; CO_2R' ; $CONHR'$; SR' ; $S(O_2)N(R')_2$; SCF_3 ; CN ; $N(R')C(O)R^4$; $N(R')C(O)OR^4$; $N(R')C(O)C(O)R^4$; $N(R')S(O_2)R^4$; $N(R')R^4$; $N(R^4)_2$; OR^4 ; $OC(O)R^4$; $OP(O)_3H_2$; or $N=CH-N(R')_2$;

Application No.: 10/622,320
Response dated March 6, 2006
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Q₂ is selected from 5-6 membered aromatic carbocyclic or heterocyclic ring systems, or 8-10 membered bicyclic ring systems consisting of aromatic carbocyclic rings, aromatic heterocyclic rings or a combination of an aromatic carbocyclic ring and an aromatic heterocyclic ring; wherein:

Q₂ is optionally substituted with up to 4 substituents, independently selected from halo, CH=N-OH, or CH=O; C₁-C₃ straight or branched alkyl optionally substituted with NR'₂, OR', CO₂R', S(O₂)N(R')₂, N=CH-N(R')₂, R³, NH-CH₃, NHCH₂CH₂OH, NHCH₂CH(OH)CH₂OH, CH₂OCH₂OCH₃, NHCH₂CH₂NH₂, NH-phenyl, piperazinyl, pyrrolidinyl or CONR'₂; O-(C₁-C₃)-alkyl optionally substituted with NR'₂, OR', CO₂R', S(O₂)N(R')₂, N=CH-N(R')₂, R³, or CONR'₂; NR'₂; OCF₃; CF₃; NO₂; CO₂R'; CONHR'; R³; OR³; NHR³; SR³; C(O)R³; C(O)N(R')R³; C(O)OR³; SR'; S(O₂)N(R')₂; SCF₃; N=CH-N(R')₂; CH=N-OH; CH=O; or CN;

wherein R' is selected from hydrogen, (C₁-C₃)-alkyl; (C₂-C₃)-alkenyl or alkynyl; phenyl or phenyl substituted with 1 to 3 substituents independently selected from halo, methoxy, cyano, nitro, amino, hydroxy, methyl or ethyl;

R³ is selected from a 5-6 membered aromatic carbocyclic or heterocyclic ring system;

R⁴ is (C₁-C₄)-alkyl optionally substituted with N(R')₂, OR', CO₂R', CON(R')₂, or SO₂N(R²)₂; or a 5-6 membered carbocyclic or heterocyclic ring system optionally substituted with N(R')₂, OR', CO₂R', CON(R')₂, or SO₂N(R²)₂;

Application No.: 10/622,320
Response dated March 6, 2006
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X is selected from -S-, -O-, -S(O₂)-, -S(O)-, [[-S(O₂)-,]]-N(R²)-, -N(R²)-S(O₂)-,

-N(R²)-C(O)O-, -O-C(O)-N(R²), -C(O)-, -C(O)O-, -O-C(O)-, -C(O)-N(R²)-, -N(R²)-C(O)-, [[

-N(R²)-,]]-C(R²)₂-, -C(OR²)₂-, -CH(OH)-;

each R is independently selected from hydrogen, -R², -N(R²)₂, -OR², SR², -C(O)-N(R²)₂, -S(O₂)-N(R²)₂, or -C(O)-OR², wherein two adjacent R are optionally bound to one another and, together with each carbon to which they are respectively bound, form a 4-8 membered carbocyclic or heterocyclic ring;

R² is selected from hydrogen, (C₁-C₃)-alkyl, or ([[C₁]]C₂-C₃)-alkenyl; each optionally substituted with -N(R')₂, -OR', SR', -C(O)-N(R')₂, -S(O₂)-N(R')₂, -C(O)-OR', or R³;

Y is selected from C or N;

A, if present, is selected from N or CR'; and

n is 0 or 1;

provided that when a compound is of formula Ig, Q₃ is 2,6-dichlorophenyl and both R substituents are H, then Q₂ is neither phenyl nor p-fluorophenyl; and

when a compound is of formula Ie, and Q₃ is 2,6-dichlorophenyl, both R substituents are H, and X is S, then Q₂ is not phenyl.

4-7. (Canceled)

8. (Previously Presented) The compound according to claim 3, wherein Q₂ is selected from phenyl or pyridyl and wherein Q₂ optionally contains up to 3 substituents, each of which is independently selected from chloro, fluoro, bromo, methyl, ethyl, isopropyl, -

Application No.: 10/622,320

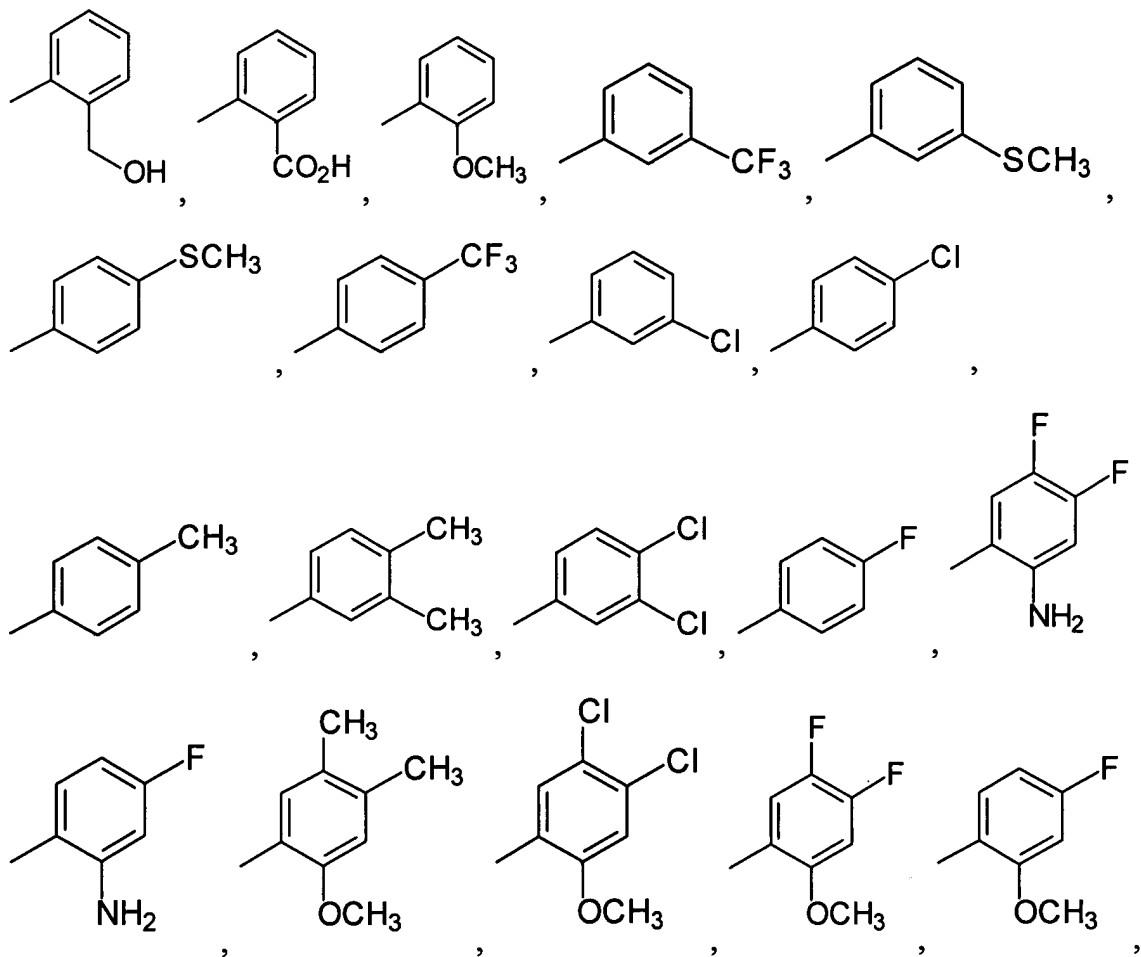
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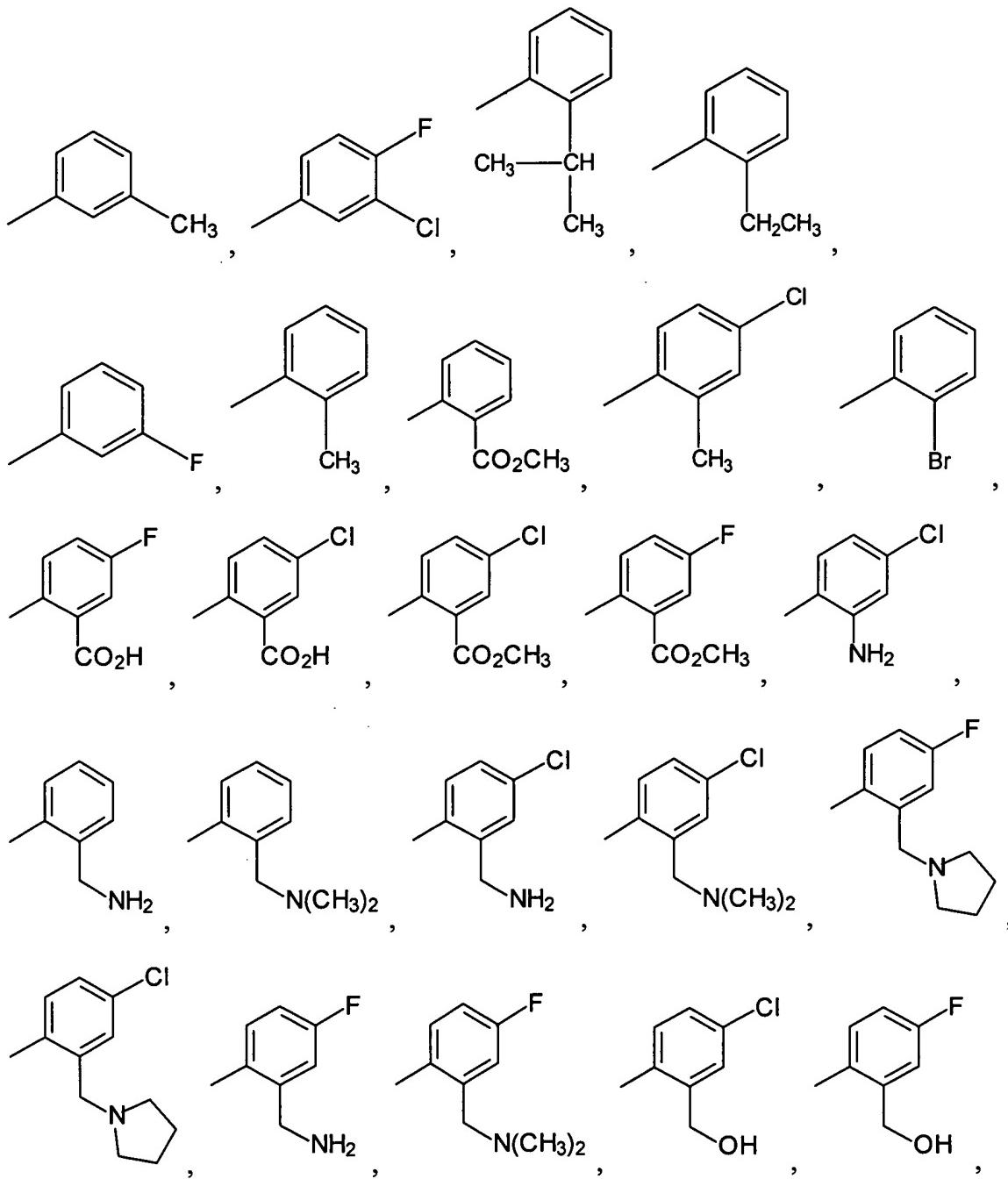
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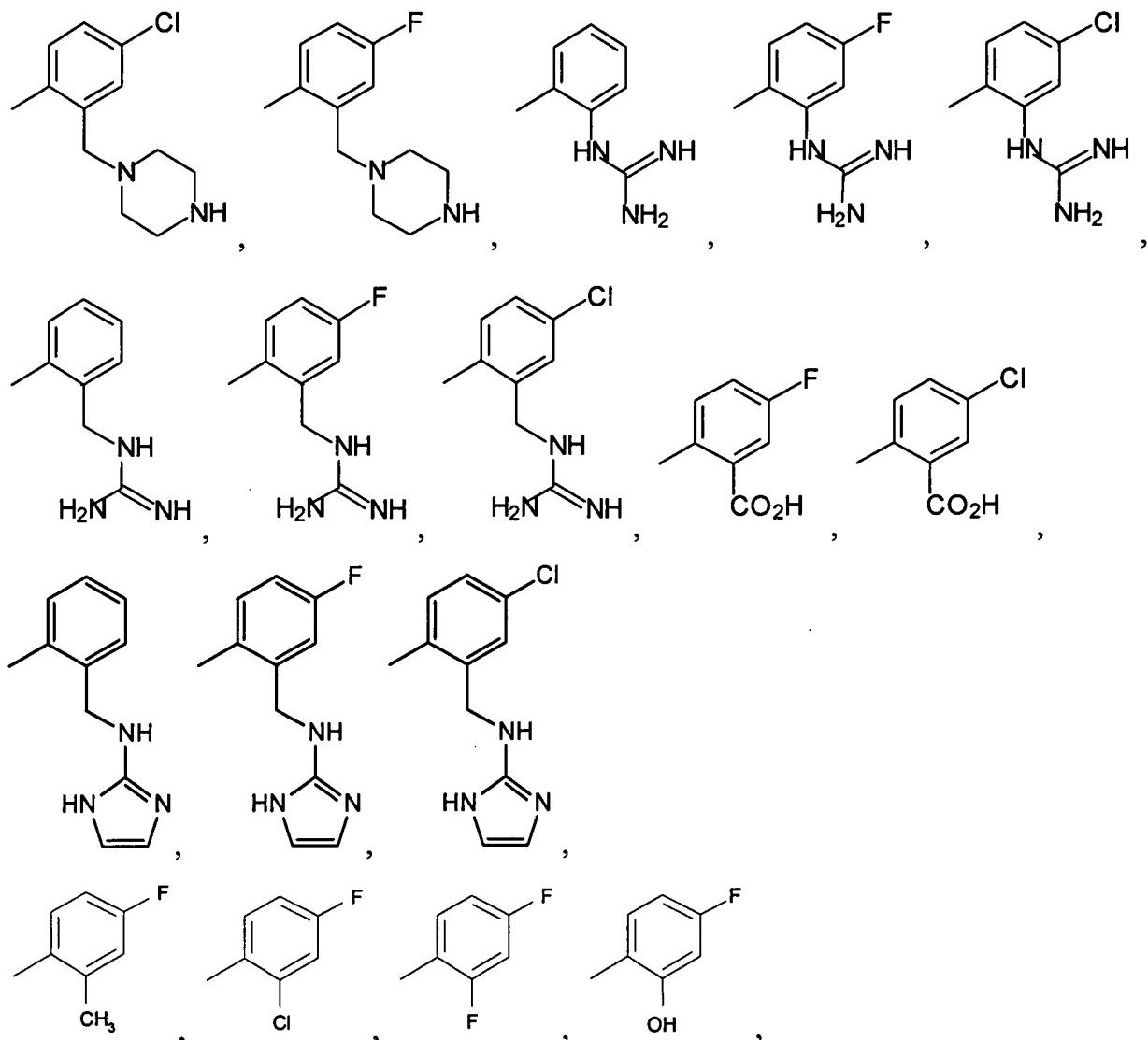
OCH₃, -OH, -NH₂, -CF₃, -OCF₃, -SCH₃, -OCH₃, -C(O)OH, -C(O)OCH₃, -CH₂NH₂, -N(CH₃)₂,

-CH₂-pyrrolidine and -CH₂OH.

9. (Previously Presented) The compound according to claim 8, wherein, Q₂ is selected from:







unsubstituted 2-pyridyl or unsubstituted phenyl.

10. (Currently Amended) The compound according to claim 9, wherein Q₂ is selected from phenyl, 2-isopropylphenyl, 3,4-dimethylphenyl, 2-ethylphenyl, 3-fluorophenyl, 2-methylphenyl, 3-chloro-4-fluorophenyl, 3-chlorophenyl, 2-carbomethoxyphenyl, 2-carboxyphenyl, 2-methyl-4-chlorophenyl, 2-bromophenyl,

Application No.: 10/622,320
Response dated March 6, 2006
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2-pyridyl, 2-methylenehydroxyphenyl, 4-fluorophenyl, 2-methyl-4-fluorophenyl,
2-chloro-4-fluorophenyl, 2,4-difluorophenyl, 2-hydroxy-4-fluorophenyl or
2-methylenehydroxy-4-fluorophenyl.

11. (Currently Amended) The compound according to claim 3, wherein X is selected from -S-, -O-, -S(O₂)-, -S(O)-, -N(R²)-, -C(R²)₂- or -C(O)-.

12. (Previously Presented) The compound according to claim 11, wherein X is S.

13-14. (Canceled)

15. (Original) The compound according to claim 14, wherein each R attached to Y is independently selected from hydrogen or methyl.

16-17. (Canceled)

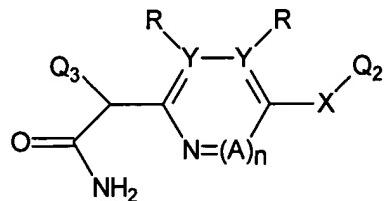
18. (Previously Presented) The compound according to claim 3, wherein Q₃ is substituted with 2 to 4 substituents, wherein at least one of said substituents is present in the ortho position relative to the point of attachment of Q₃ to the rest of the inhibitor.

19. (Original) The compound according to claim 18, wherein both ortho positions are occupied by one of said independently selected substituents.

20. (Original) The compound according to claim 19, wherein Q₃ is a monocyclic carbocyclic ring; and each of said ortho substituents on Q₃ are independently selected from halo or methyl.

21. (Previously Presented) The compound according to claim 19, wherein Q₃ contains 1 to 2 substituents in addition to said ortho substituents, said additional substituents being independently selected from NR'₂, OR', CO₂R', CN, N(R')C(O)R⁴; N(R')C(O)OR⁴; N(R')C(O)C(O)R⁴; N(R')S(O₂)R⁴; N(R')R⁴; N(R⁴)₂; OR⁴; OC(O)R⁴; OP(O)₃H₂; or N=CH-N(R')₂.

22. (Previously Presented) The compound according to claim 3, wherein said compound is a compound of formula Ie:

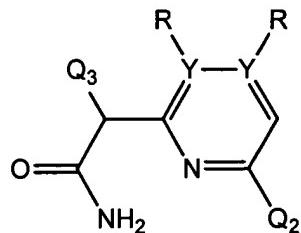


and is selected from any one of the following compounds:

Application No.: 10/622,320
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 Reply to Office Action of September 6, 2005

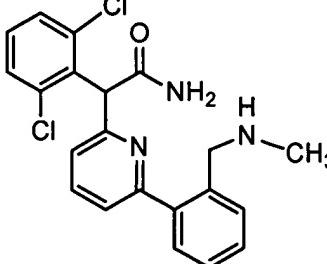
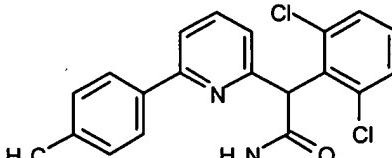
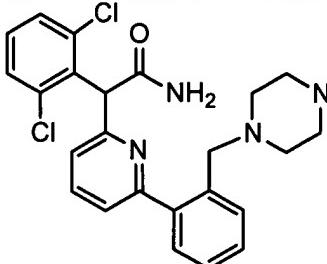
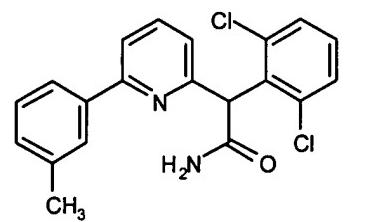
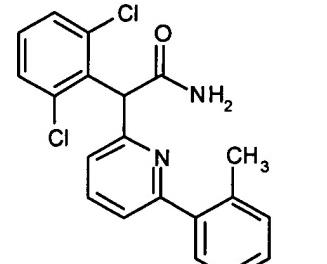
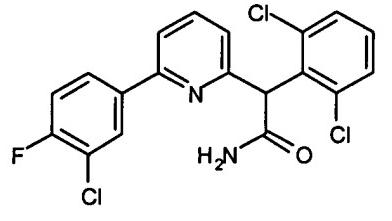
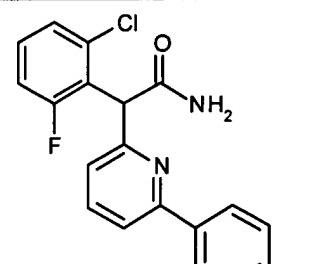
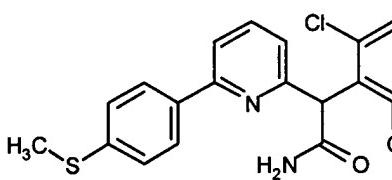
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23. (Previously Presented) The compound according to claim 3, wherein said compound is a compound of formula Ig:

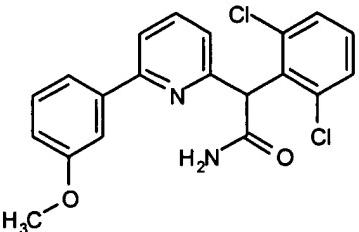
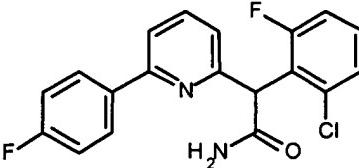
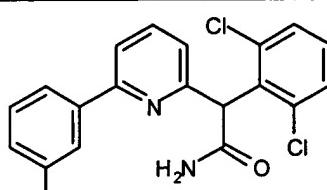
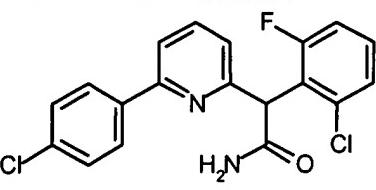
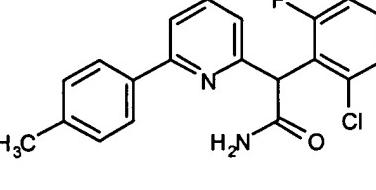
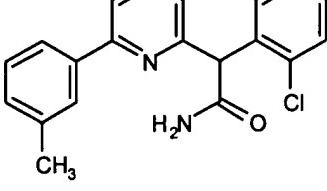
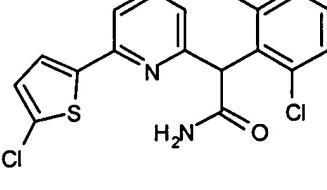
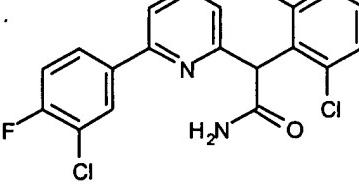


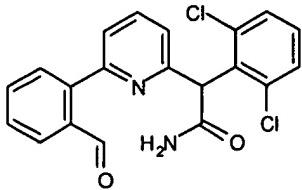
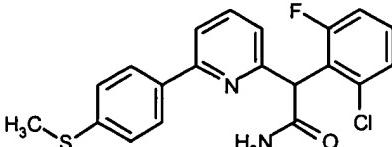
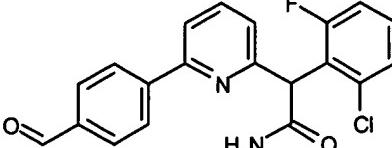
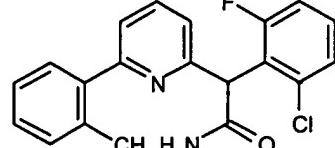
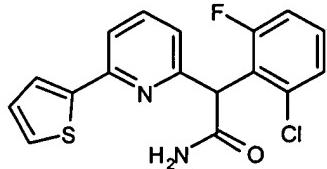
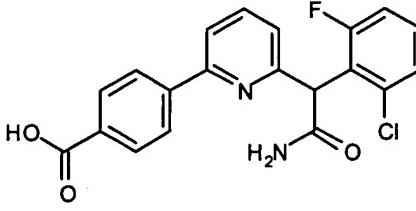
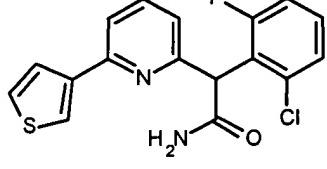
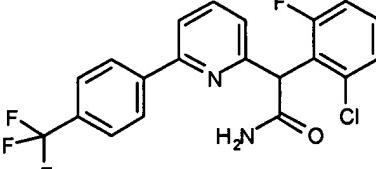
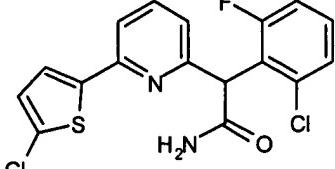
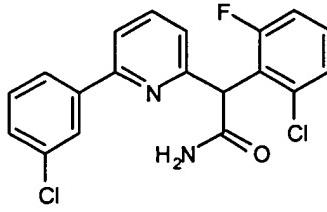
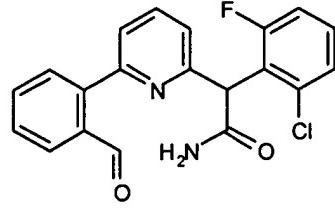
and is selected from any one of the following compounds:

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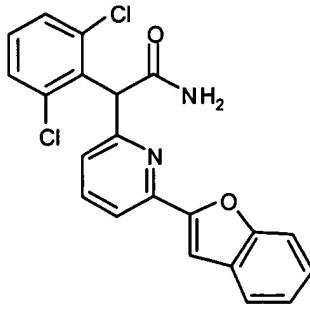
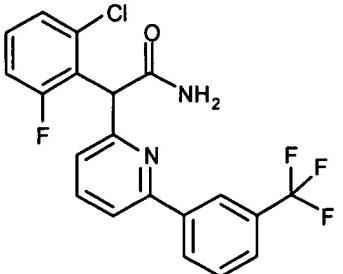
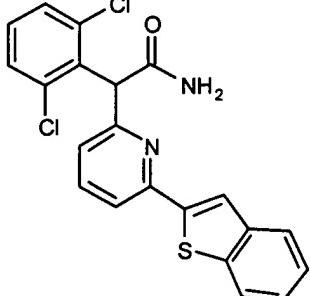
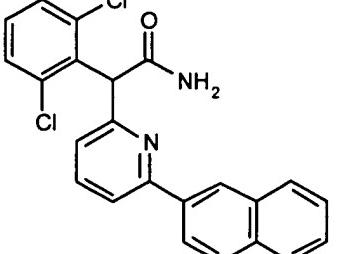
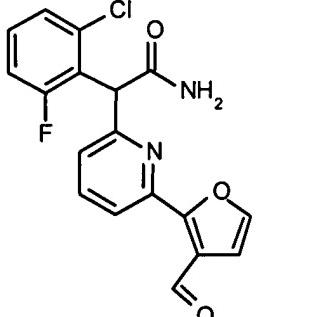
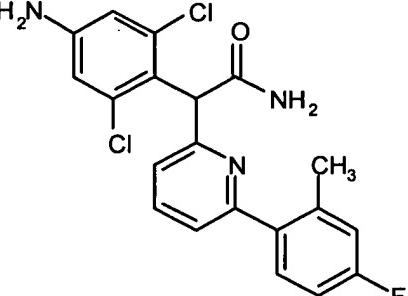
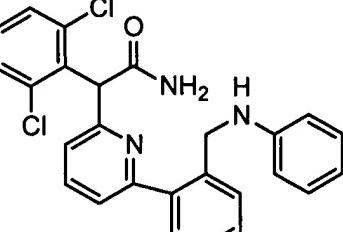
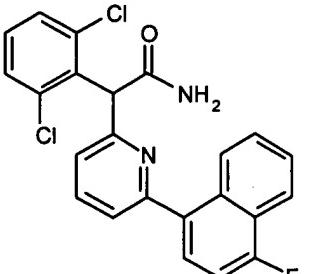
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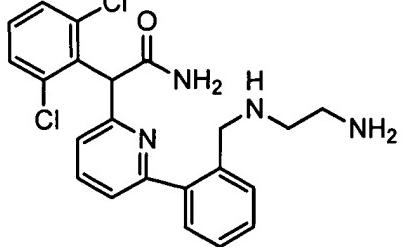
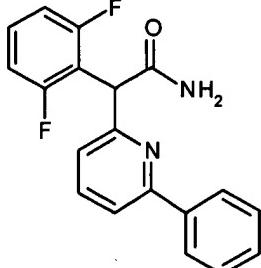
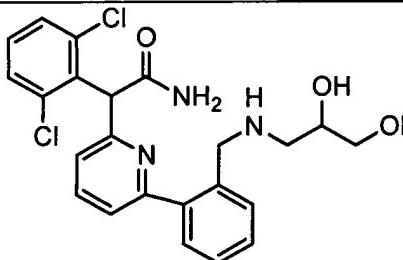
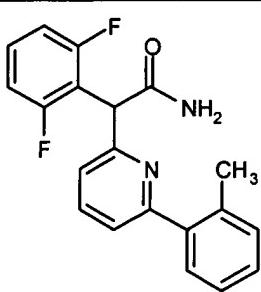
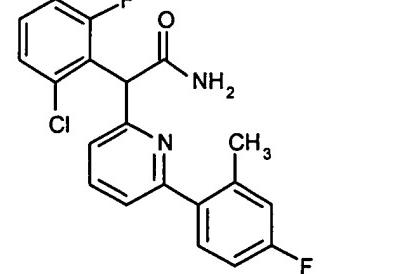
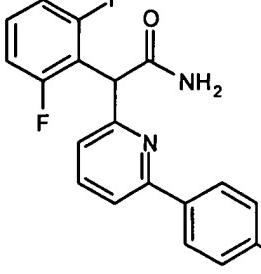
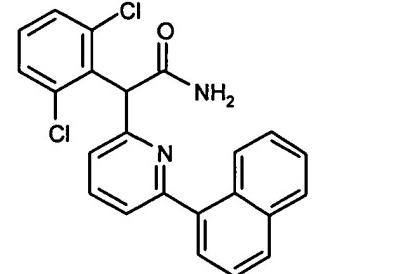
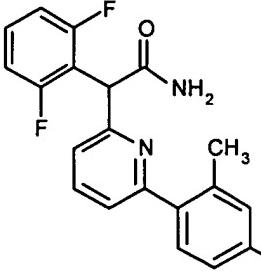
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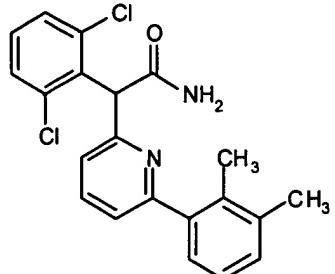
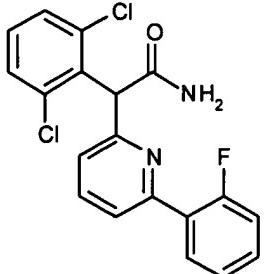
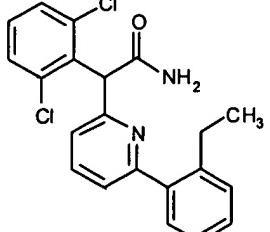
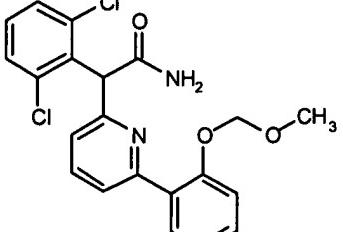
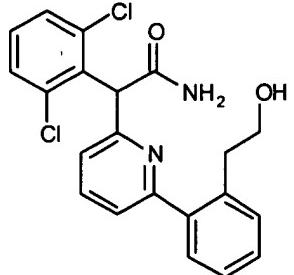
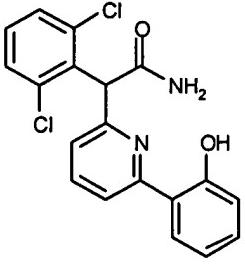
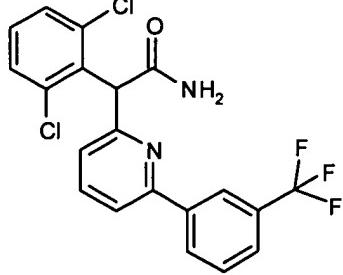
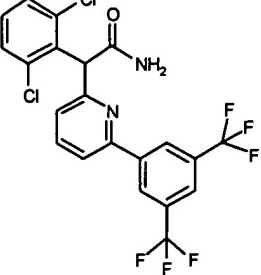
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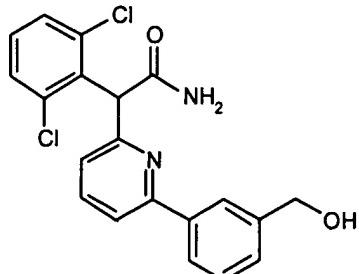
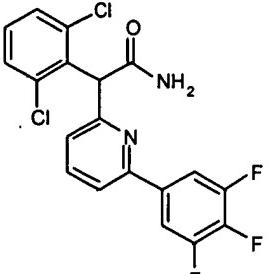
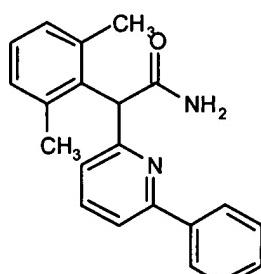
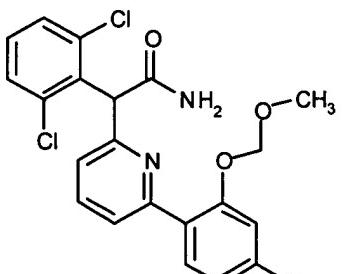
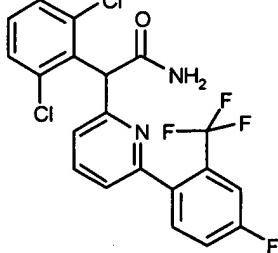
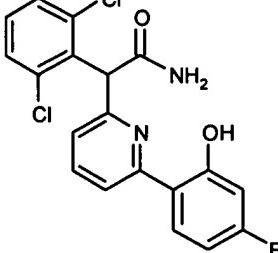
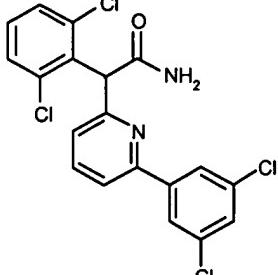
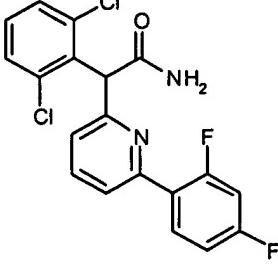
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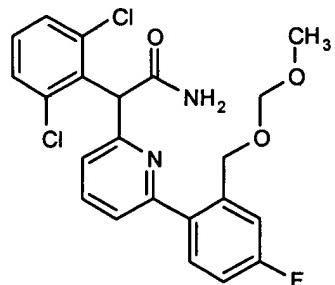
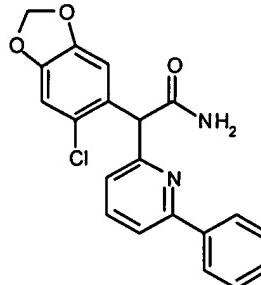
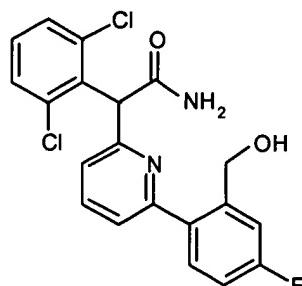
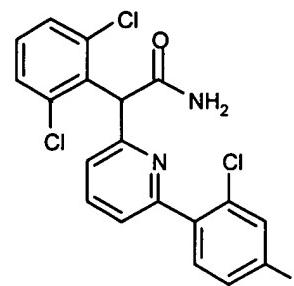
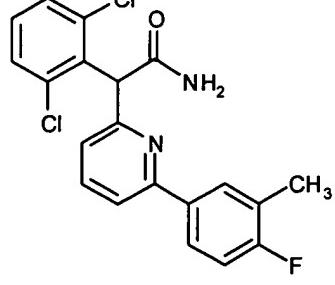
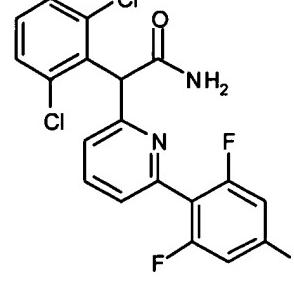
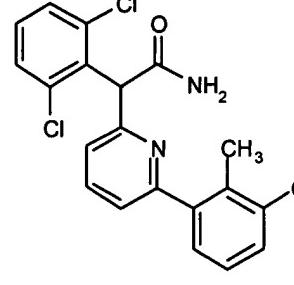
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24. (Canceled)

25. (Previously Presented) A pharmaceutical composition comprising an amount of a compound according to claim 3 effective to inhibit p38, and a pharmaceutically acceptable carrier.
26. (Currently Amended) A method of treating or preventing inflammatory diseases, autoimmune diseases, viral diseases, destructive bone disorders, proliferative disorders, infectious diseases, neurodegenerative diseases, allergies, reperfusion/ischemia in stroke[[or]], myocardial ischemia, renal ischemia, heart attacks, angiogenic disorders, organ hypoxia, vascular hyperplasia, cardiac hypertrophy, thrombin induced platelet aggregation or conditions associated with prostaglandin endoperoxide synthase-2, rheumatoid arthritis, inflammatory bowel disease, ulcerative colitis, or Crohn's disease in a patient, said method comprising administering to said patient a composition according to claim 25.
27. (Currently Amended) The method according to claim 26, wherein said use is method is used to treat or prevent an inflammatory disease selected from acute pancreatitis, chronic pancreatitis, asthma, allergies, or adult respiratory distress syndrome.
28. (Currently Amended) The method according to claim 26, wherein said use is method is used to treat or prevent an autoimmune disease selected from glomerulonephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis,

Application No.: 10/622,320

Response dated March 6, 2006

Reply to Office Action of September 6, 2005

~~myasthenia gravis, multiple sclerosis, inflammatory bowel disease, ulcerative colitis, or Crohn's disease, psoriasis, or graft vs. host disease.~~

29. (Currently Amended) The method according to claim 26, wherein said ~~use is method is used to treat or prevent~~ a destructive bone disorder selected from osteoarthritis, osteoporosis or multiple myeloma-related bone disorder.

30-33. (Canceled)

34. (Currently Amended) The method according to claim 26, wherein said ~~use is method is used to treat or prevent~~ ischemia/reperfusion in stroke[[or]], myocardial ischemia, ~~or renal ischemia, heart attacks, organ hypoxia or thrombin-induced platelet aggregation.~~

35-37. (Canceled)